MAIL STOP RCE

Attorney Docket No. 27550U

In re Application of:

Jacob HOCHMAN		Conf. No.	9817
Application No.	10/587,835	Art Unit:	1643
Filed	Sep. 20, 2006	Examiner:	HOLLERAN, Anne L.

For: METHOD FOR DIAGNOSING AND TREATMENT OF BREAST CANCER AND PHARMACEUTICAL COMPOSITION AND KIT OF SAME

DECLARATION UNDER 37 CFR § 1.132

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

Dear Commissioner:

I, Jacob Hochman, declare as follows:

1. I am employed as a Professor of Cell Biology at the Institute of Life Sciences, The Hebrew University of Jerusalem, Jerusalem, Israel, and engaged in Cancer Research and Development, and Teaching. I have been in my current position since 1970. My responsibilities include Laboratory head, directing research of graduate and post-graduate students, as well teaching various courses at the undergraduate and graduate levels. I am also a member of various university committees. Currently, I am a member of the Faculty of 1000 (F1000) in Experimental Cancer Therapy. I also serve on Israeli National Grant Reviewing Committees in Immunology and Cancer Research. I also serve as reviewer for various scientific journals. From 2001-2006: I was a Fogarty Scholar at the National Institutes of Health (NIH), Bethesda, Maryland. Prior to that, from 1980-1981 and from 1986-1987 I was a visiting scientist at the National Institutes of Health (NIH), Bethesda,

Maryland (Regulation of Cancer Growth and Metastasis). Prior to that, from 1974-1975, I was a visiting professor at the University of California, San Francisco campus, San Francisco, California (Somatic Cell Genetics).

2. **Academic credentials:** I received my B.Sc, M.Sc and Ph.D degrees from the Hebrew University of Jerusalem I have reviewed the specification of United States Patent Application No. 10/587,835. I am an inventor of the subject matter claimed.

3. I have reviewed the amended claims. In this regard, independent claim 40 is directed to a "A method for diagnosing breast cancer in a subject comprising determining levels of expression of p14 peptide in one or more samples from said subject, a high level of expression signifying a high probability for breast cancer in said subject, wherein the sample is a fluid sample." Claims 41-44 each depend, either directly or indirectly, from claim 40. Independent claim 47 is directed to "A method for screening of fluid samples from subjects into those that have a relatively high probability of having or being susceptible of developing breast cancer and those that have a relatively lower probability of having or being susceptible of developing breast cancer, the method comprising contacting the samples with anti-p14 antibodies and determining binding of anti-p14 antibodies and p14 peptide if in said sample, a high degree of binding signifying a corresponding higher probability of having or being susceptible of developing breast cancer". Claims 48 and 49 each depend either directly or indirectly from claim 47.

4. I have also studied the Official Action issued on December 11, 2010 in the present application. In particular, at pages 4 to 6 of the Official Action, claims 40 to 44 and 47 to 50 remain rejected under 35 USC § 103, the Examiner asserting that the invention is unpatentable over Pogo, in view of Hoch-Marchaim and further in view of Melana I or Melana II.

5. However, in contrast to the assertions of the Examiner in the Official Action, and considering the limitation of the tested sample to bodily fluid sample, in particular blood serum, it is my belief and understanding that the specification is inventive over the cited art.

6. As evidence of the detection of p14 in a fluid sample rather than in the cancerous tissue, I have overseen the preparation of and studied the experiments and data described herein below. The data described herein provides evidence that p14 is present in sera from mice previously injected with 4T1 (murine mammary carcinoma that harbors MMTV) or T-67 (murine lymphoma that harbors MMTV, descendants of T-25) cells.

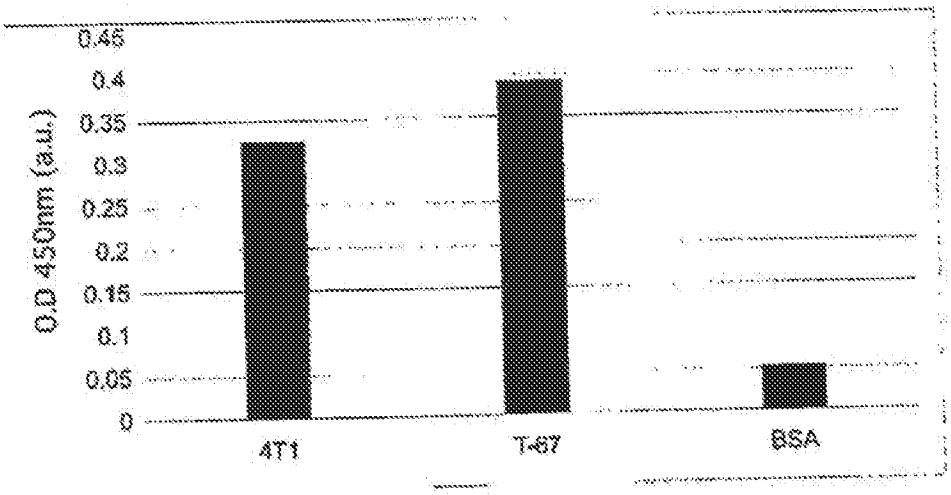
7. Specifically, the following experiment has been conducted: Maxisorp ELISA plates (NUNC, Denmark) were coated with either 1 μg/ml of purified recombinant p-14 protein (control) or with sera from mice previously injected with 4T1 (murine mammary carcinoma that harbors MMTV) cells or with T-67 (murine lymphoma that harbors MMTV, descendants of T-25) cells (in 0.1M carbonate buffer pH 9.6).

8. All plates were incubated overnight at 4ºC and then blocked for 2 hours at room temperature with a blocking buffer containing 3% BSA and 0.05% Tween 20 in phosphate buffered saline (PBS, 0.1M phosphate buffer, 150 mM NaCl, pH 7.2). Polyclonal Rabbit anti p-14 antibody was added (100μl) to the serum-coated wells. Plates were incubated for 2 hours at room temperature. The wells were washed 3 times with 200μl PBS containing 0.05% Tween 20 and 100 μl of horseradish peroxidase(HRP)-conjugated 2^{nd} Ab (anti-mouse or anti-rabbit, respectively) diluted 1:10,000 in blocking buffer were added to each well. After an additional incubation for one hour at room temperature and washing, as above, the bound HRP-conjugate was detected by adding 100 μl of tetramethyl benzidine. The peroxidase reaction was stopped after 5 minutes by the addition of 50 μl 0.5M H_2SO_4. Optical densities at 450 nm were measured using an ELISA plate reader.

9. Figure 1 depicts the presence of p14 in the serum of mice inoculated with 4T1 mammary carcinoma or T-67 lymphoma, both harboring MMTV.

10. At the time of filing the application it was known that the leader peptide of the Env-precursor of MMTV, while present in the cytoplasm, is translocated to and concentrated within the nucleoli of murine T-cell lymphomas that harbor this virus [from background of application making reference to Hoch-Marchaim, H., et al. Virology, 242:246-254, 1998; Hoch-Marchaim, H.,

Virology, 313:22-32, 2003).



11. Thus, it was unexpected that the p14 be detected in bodily fluids, such as a blood sample and that, this may be used as a tool for detecting and screening of breast cancer patients.

12. I herby further declare that the statement made herein of my own knowledge is true; and further that this statement was made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 81 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Jacob Hochman

DECLARANT NAME

Jacob Hochman

Date

March 30, 2011